

## REMARKS

The communication responds to the Office Action of December 27, 2007 in which the Examiner rejected Claims 1, 32-35, 52, and 64 under 35 U.S.C. § 112 and Claims 1, 32-35, 52, and 64 under 35 U.S.C. § 103. In view of the following remarks, the Applicant respectfully requests reconsideration and allowance of the pending claims.

### General Matters

In response to the Examiner's request at item 4, first bullet point, the Applicant confirms that the Office Action mailed on August 11, 2006 for the present matter was, in fact, mailed on August 11, 2006 rather than August 11, 2005 or September 11, 2006.

In the second bullet point, the Examiner referenced items 13 and 14 of page 13 of the office action of July 27, 2007. Item 13 is reproduced below:

In responding to the rejections under 35 U.S.C. 112, 2<sup>nd</sup> paragraph in Office Action mailed 11 August 2006, applicant repeated (sic) refers "Examiner objected to" (See Page 15, Lines 18, 22 and 27 and Page 6, Line 5). Applicant to note that. (sic) Claim 1 was not objected to, rather, Claims 3, 32-35, 52 and 64-65 were objected to in the Office Action mailed 11 August 2006 (e.g., See page 4, Line 19).

The Applicants note the section referred to by the Examiner addresses the rejection made by the Examiner under 35 U.S.C. 112, second paragraph. That rejection applied to Claims 1, 30, 32-35, 52, and 64-65. Accordingly, claim 1 was properly included in the Applicant's response. By way of clarification, the Applicant submits that the Applicant intended to refer to the Examiner's rejection of, among others, claim 1.

Item 14 is also reproduced:

Applicant has discussed objection of Claim 8 in response filed 11 December 2006 (See response Page 16, Line 3-4). Claim 8 has been withdrawn from consideration (See Office Action mailed 11 August 2006, Page 4, item 8, Line 1). Appropriate correction to the record is required.

The portion of the Office Action response referred to by the Examiner in fact sets forth that the Examiner objected to a withdrawn claim: “The Examiner objected to Claim 8 as incomplete. Applicants respectfully note that Claim 8 is not currently pending in the application.” The Applicant did not address the Examiner’s objection because claim 8 is not pending in the application. The Applicant respectfully requests clarification as to what correction of the record is thus required.

The third bullet point states: “Confusion between objection and rejection as mentioned at item 15.” The Applicant respectfully submits that this is addressed with respect to item 13, reproduced above.

Claim Rejections Under 35 U.S.C. § 112

The Examiner states repeatedly throughout the office action that the claims are drawn to a method to sterilize a biological material in the presence of a “protective atmosphere” comprised of an “inert,” or a mixture of an “inert” and a reducing atmosphere. See, e.g., Page 5, Page 6, Page 7. The Applicant notes that the Examiner has erroneously characterized the Applicant’s claimed invention by reversing the use of inert and reducing atmospheres. In contrast, Applicant notes that Claim 1 recites, in part, “providing a protective atmosphere . . . wherein providing a protective atmosphere . . . is carried out by at least partially removing an original atmosphere under vacuum, and replacing the original atmosphere with a reducing atmosphere or a mixture of an inert atmosphere and a reducing atmosphere.”

Claims 1, 32-35, 52, and 64 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Similarly, Claims 1, 32-35, 52, and 64 were rejected under 35 U.S.C. § 112, first paragraph, with the Examiner asserting that the specification, while being enabling for a method to sterilize a biological material in presence of a “protective atmosphere” comprised of an “inert” or mixture of an “inert” and reducing atmosphere does not provide evidence for a sterilizing method with the step to reduce and/or inactivate an adventitious agent or adventitious agents. The Examiner asserts the structure of the claimed invention does not fit the description presented because there is no clear evidence/data showing reduction and/or inactivation of an adventitious agent or adventitious agents and that the physical and chemical aspects for reduction and/or inactivation of an adventitious agent or

adventitious agents is not of record in the specification. See, Page 5. The Applicant respectfully traverses the rejections for at least the following reasons.

Currently amended Claim 1 recites, in part, “sterilizing the packaged biological material in the presence of said protective atmosphere to reduce and/or inactivate an adventitious agent or adventitious agents.” In contrast to the Examiner’s assertion, Applicant’s specification fully discloses and supports “sterilizing the packaged biological material:”

The terms “sterilizing,” “sterilization” and terms of like import shall be understood herein to mean a significant reduction in the bioburden of a biological material by the destruction and/or deactivation of adventitious agents such as microorganisms, particularly pathogenic bacterial and viral microorganisms, and polynucleotide fragments thereof present upon and/or within the biological material. Para. [0026] (emphasis added).

Although with specific reference to optional procedures that the biological material may be subjected to prior to packaging, Applicant provides several examples of reducing the bioburden of the biological material:

... reducing the bioburden of the biological material, e.g., subjecting the biological material to an ionizing radiation dose of from about 2 to about 50 kGy and preferably from about 5 to about 25 kGy, subjecting the biological material to ultraviolet radiation of from about 1 nm to about 400 nm for from about 1 minute to about 1 hour and preferably from about 5 minutes to about 30 minutes, subjecting the biological material to pasteurization at from about 60 to about 120° C. for from about 1 minute to about 1 hour and preferably from about 90 to about 110° C. for from about 1 minute to about 5 minutes, and/or contacting the biological material with a bioburden-reducing amount of at least one antibiotic agent, antiviral agent and/or antimycotic agent selected from the group consisting of amphotericin B, gentamycin sulfate, imidazole compounds, azole compounds, such as ketoconazole, miconazole nitrate and aliphatic hydroxy acids, their salts and their glycols. Para. [0032] (emphasis added).

Applicant similarly discusses the sterilization step following packaging of the biological material:

The step of irradiating the packaged biological material can be achieved by subjecting the biological material to a total dose of

radiation of from about 2 to about 50 kGy and preferably from about 5 to about 25 kGy . . . Para. [0036].

The radiation employed in irradiating step (c) herein is typically an ionizing radiation. Para. [0039].

The three types of ionizing radiation used herein are: gamma, electron beam (E-beam) and X-ray. Para. [0041].

It is understood that biological materials can be effectively sterilized by gamma, electron-beam, or X-ray radiation. Para. [0046] (emphasis added).

The Applicant submits that, for example, radiation is an accepted sterilization process known to those skilled in the art. The inventive concept of a reducing gas protection process may be applied to a radiation dosage as would be known to one skilled in the art, using known methods.

The Applicant thus submits that the application discloses and supports “sterilizing the packaged biological material,” as recited in Claim 1. Furthermore, Applicant discloses how to determine the reduction in bioburden of the biological material:

Bioburden determinations can be carried out to determine a desired radiation dose. Thus, the dosage of ionizing radiation for a specific bioactive material can be experimentally determined by measuring the bioburden of the pre-sterilized material employing known and conventional procedures so as to provide a typical range of initial bioburden for the material and thereafter irradiating portions of the material at different dosage levels and again measuring bioburden following termination of each radiation exposure. Based on these experimental data, an optimum radiation dosage level can be determined for a specific biological material and target bioburden endpoint. In these experiments, radiation exposure can be monitored with biological indicators utilizing *Bacillus pumilus* as the test organism. Counters and electronic measuring devices can also be used. Chemical dosimeters based on ferrous sulfate, ferrous cupric sulfate, or ceric sulfate are also generally useful. Color-change process indicators may be used but these cannot measure the radiation dose.

In general, the radiation exposure whether for gamma rays, E-beam or X-rays, can range from about 5 to about 50 kGy and preferably from about 10 to about 40 kGy depending on the nature of the biological material to be sterilized, its initial bioburden and the desired bioburden endpoint. Paras. [0057]-[0058].

Additionally, Applicant provides several examples in Paragraphs [0063]-[0077] that are “illustrative of the method for sterilizing a bioactive material in accordance with the invention.” Para. [0062].

Thus, Applicant provides full disclosure and support for “sterilizing the packaged biological material in the presence of said protective atmosphere to reduce and/or inactivate an adventitious agent or adventitious agents.” Particularly, Applicant discloses sterilizing the packaged biological material, which is expressly defined in Applicant’s specification as a significant reduction in the bioburden of a biological material by the destruction and/or deactivation of adventitious agents, Applicant discloses several methods of reducing the bioburden, including irradiating the biological material, and Applicant discloses a method of determining the reduction in bioburden. In contrast to the Examiner’s assertion, undue experimentation would not be required for one of ordinary skill in the art to practice the invention, as Applicant has fully disclosed how to achieve each of the limitations of the pending claims.

The Examiner further asserts that the phrase “a therapeutically useful device,” as used in Claim 64, is not an art-recognized “biological material,” and therefore the definition of “biological materials” as presented in the described specification is not consistent with art-recognized terminology/definition. See, Page 6. Applicant respectfully points the Examiner to the MPEP, which recites “[c]onsistent with the well-established axiom in patent law that a patentee or applicant is free to be his or her own lexicographer, a patentee or applicant may use terms in a manner contrary to or inconsistent with one or more of their ordinary meanings if the written description clearly redefines the terms.” MPEP § 2173.05(a) (emphasis added) (citing *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357 (Fed. Cir. 1999)). While Applicant does not believe that the use of the term “therapeutically useful device” in Claim 64 is inconsistent with art-recognized “biological materials,” Applicant, in Paragraph [0023], has expressly defined the term “biological material” to apply to “any food or medically/surgically useful substance or device having a therapeutic action directly involving at least one biological mechanism and is to be distinguished from a biologically inert substance or device whose medical/surgical usefulness is essentially of a physical or mechanical character” (emphasis

added). Therefore, Applicant's uses of the terms "therapeutically useful device" and "biological material" are appropriate.

Reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph are respectfully requested.

Claims 1, 32-35, 52, and 64 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Applicant respectfully traverses the rejection for at least the following reasons.

The Examiner asserts that Claim 1 is incomplete "because said claim does not elaborate each and every element of the step about accomplishing to have protected one or more property (sic) of a biological material." Page 9. 35 U.S.C. § 112, second paragraph, requires that "[t]he specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." Applicant respectfully asserts that amended Claim 1 clearly meets all limitations required by 35 U.S.C. § 112, second paragraph, by calling for a method comprising, in part, "a) packaging the biological material; b) providing a protective atmosphere within the package . . . and c) sterilizing the packaged biological material . . ." Even the Examiner indicates "there is no specific rule or statutory requirement that specifically addresses the need for a detailed step in claims in a process." Therefore, Applicant respectfully asserts that the Examiner's assertion that Claim 1 is incomplete is in error.

The Examiner asserts there is insufficient antecedent basis for the limitations "package" and "packaged biological material" in Claim 1, step b). According to MPEP § 2173.05(e), "[o]bviously, however, the failure to provide explicit antecedent basis for terms does not always render a claim indefinite. If the scope of a claim would be reasonably ascertainable by those skilled in the art, then the claim is not indefinite." Applicant notes that one skilled in the art would clearly recognize that "packaging the biological material," as recited in step a) of Claim 1, would result in a "package" and "packaged biological material." Applicant respectfully asserts that attempting to clarify the antecedent basis with additional language would only make the claim more difficult to understand.

The Examiner further asserts that the phrases “inert atmosphere” in Claims 1, 32, and 34 and “inert gas” in Claim 32 render those claims incomprehensible, unclear, and vague because the metes and bounds for the word “inert” are not delineated. The Examiner has indicated that one skilled in the art would have “[a]t least a Bachelor Degree in Biochemical engineering, Biochemistry, Biology, Biomedical engineering, Biophysics, Chemical engineering, Chemistry, Cytology, Environmental engineering, Environmental Science and Technology, Histology, Material Science and engineering, Microbiology, Molecular biology, Pharmaceutical Sciences, or Pharmacology.” The Applicant respectfully asserts that one skilled in the art, and particularly one skilled in the art as defined by the Examiner, will readily recognize the meaning of the term “inert” as it is used in Claims 1, 32, and 34. Applicant further points the Examiner to the MPEP, which recites “[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow.” MPEP § 2111.01(I) (emphasis added) (citing *In re American Academy of Science Tech Center*, 367 F.3d 1359, 1369, (Fed. Cir. 2004)). Additionally, “[i]n applying the prior art, the claims should be construed to encompass all definitions that are consistent with applicant's use of the term. MPEP § 2173.05(a)(III) (emphasis added) (citing *Tex. Digital Sys., Inc. v. Telegenix, Inc.*, 308 F.3d 1193, 1202 (Fed. Cir. 2002)).

The Examiner additionally asserts the phrase “therapeutically useful device” as part of a Markush group consisting of a “biological material” in Claim 64 renders said claim incomprehensible, unclear, vague, and therefore, indefinite. Particularly, the Examiner questions how a “biological material” can be a “therapeutically useful device.” In addition to Applicant’s comments above relating to Applicant’s appropriate uses of the terms “therapeutically useful device” and “biological material,” Applicant further directs the Examiner to Paragraph [0027] of Applicant’s specification, wherein Applicant explains that preferred biological materials include cancellous and corticocancellous bone implantable devices which possess osteogenic and/or osteoconductive properties. As such, Applicant has provided at least one example of how a “biological material” can be a “therapeutically useful device.”

Reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph are respectfully requested.

Claim Rejections under 35 U.S.C. § 103

Claims 1, 32-35, 52, and 64 were rejected under 35 U.S.C. § 103(a) as obvious over the combined teachings from Sierra et al. (WO 98/31403) in view of Schankereli (US 5,782,914) and further in view of Bertiger (US 4,538,757). Applicant respectfully traverses the rejection for at least the following reasons.

None of the references, alone or in combination, teach or suggest “providing a protective atmosphere within the package, wherein providing a protective atmosphere within the packaging of the packaged biological material is carried out by at least partially removing an original atmosphere under vacuum, and replacing the original atmosphere with a reducing atmosphere or a mixture of an inert atmosphere and a reducing atmosphere, and sterilizing the packaged biological material in the presence of said protective atmosphere to reduce and/or inactivate an adventitious agent or adventitious agents.”

The Examiner states that Sierra et al. do not teach that radiation sterilization is conducted in the presence of an inert gas mixed with a reducing atmosphere or in the presence of a reducing atmosphere. Page 11. Again, Applicant notes that the Examiner has erroneously characterized Applicant’s claimed invention by reversing the use of inert and reducing atmospheres. In contrast, Applicant notes that Claim 1 recites, in part, “providing a protective atmosphere . . . wherein providing a protective atmosphere . . . is carried out by at least partially removing an original atmosphere under vacuum, and replacing the original atmosphere with a reducing atmosphere or a mixture of an inert atmosphere and a reducing atmosphere.” Sierra et al. do not teach or suggest “partially removing an original atmosphere under vacuum, and replacing the original atmosphere with a reducing atmosphere or a mixture of an inert atmosphere and a reducing atmosphere.”

Schankereli does not remedy the disclosure deficiencies of Sierra et al. Schankereli discloses a method for preparing heterogeneous graft material. Col. 1, ll. 8-9. Vacuum-dried tissue specimens are inserted into a moisture-proof sterilizing pouch, which may be evacuated. Col. 3, ll. 57-58. Schankereli discloses evacuation and/or replacement of the atmosphere within the tissue package (the package containing the dried tissue) using a media such as argon or nitrogen limits free radical formation (oxidation) of the tissue during the sterilization process.

Nonetheless, Schankereli does not teach or suggest “replacing the original atmosphere with a reducing atmosphere or a mixture of an inert atmosphere and a reducing atmosphere,” as recited in Applicant’s Claim 1.

The Examiner has relied on Bertiger for teaching exposure of material to be processed to a mixture of an inert atmosphere and a reducing atmosphere. Applicant respectfully asserts that the combination of Sierra et al. and Schankereli with Bertiger is improper. Bertiger discloses a method and apparatus for wave soldering in a reducing atmosphere which prevents oxide formation and provides a fluxing action. Col. 1, ll. 6-11. The Bertiger apparatus and method for wave soldering eliminates the steps of fluxing and flux cleaning present in prior art wave soldering devices. Col. 3, ll. 4-6. A wave soldering apparatus 10 is contained primarily within an enclosure 12 having an entrance 13 and an exit 14. Col. 2, ll. 4-6. The atmosphere inside enclosure 12 is further controlled by an atmosphere supply apparatus 27 comprising a nitrogen gas supply 26, a hydrogen gas supply 28, a proportioning valve 29, and a gas inlet 30. Col. 2, ll. 25-28. Valve 29 controls the proportions of the gases in the mixture supplied to enclosure 12 by means of inlet 30 so that the mixture comprises approximately 85% by volume of nitrogen and approximately 15% by volume of hydrogen. Col. 2, ll. 28-33. The hydrogen in the gas mixture fed to enclosure 12 provides a fluxing action during the wave soldering procedure. Col. 2, ll. 41-43. This allows the entire wave soldering procedure to be carried out in a non-oxidizing atmosphere. Col. 2, ll. 53-54. A conveyor apparatus 15 runs through enclosure 12 by means of entrance 13 and exit 14. Col. 2, ll. 7-9. In use, articles 17, 18, 19, and 20 are carried on conveyor apparatus 15 through enclosure 12. Col. 2, ll. 9-10.

The Applicant notes that, typically, during many forms of sterilization suitable for use with the protective atmosphere, there is no heat. Reaction of hydrogen is directly with free radicals. This may be contrasted with wave soldering; wave soldering relies on heat to remove oxidation products from metal. Thus, the concerns that arise with wave soldering may be widely variant from those that arise during irradiation, for example. With respect to irradiation in particular, hydrogen can react from free radicals from any source, including oxygen compounds in tissue (such as lipids). This may be contrasted with merely removing oxygen from air, for example by vacuum packaging. Vacuum packaging relies on vacuum to reduce oxygen content and so minimize oxidization. Vacuum packaging, however, will not remove oxygen compounds

from tissue. It is for at least this reason that a protective atmosphere, such as a reducing gas atmosphere, may be useful.

The Applicant respectfully submits that the Examiner is using Applicant's invention as a template through a hindsight reconstruction of Applicant's Claim 1 to merely piece together references disclosing each of the limitations of Applicant's Claim 1, separately and independently, to arrive at Applicant's novel and advantageous method of protecting one or more properties of biological material during the process of sterilization. Bertiger has no relevance to the disclosures of Sierra et al. and Schankereli, which relate to the preparation and use of biological materials. Bertiger discloses wave soldering of printed circuit boards, for example, as they are run through an unevacuated enclosure 12 on a conveyor belt. No materials are packaged and sterilized. In fact, Bertiger does not disclose any need for packaging and sterilizing articles 17, 18, 19, and 20, instead disclosing that once past the soldering apparatus, the articles are moved out of enclosure 12 by means of exit 14, back to the external atmosphere. Bertiger discloses only that the use of a nitrogen and hydrogen mixture allows a wave soldering procedure to be carried out in a non-oxidizing atmosphere and removes the need for a conventional fluxing agent. Removing articles from the non-oxidizing atmosphere and back into the external atmosphere would defeat the purpose of sterilization, which is the focus of Applicant's Claim 1. The Examiner has not provided sufficient reason or explicit analysis of why the disclosures of Sierra et al. and Schankereli should be combined with Bertiger. The Examiner has merely provided the conclusory statement that "each of Schankereli and Bertiger substantiate Sierra et al.'s teachings since each one of Schankereli and Bertiger teach preventing oxidation of the material being processed because of the interaction of heat produced during each of the gamma irradiation or soldering."

Therefore, Claim 1 is not made obvious by Sierra et al. in view of Schankereli and Bertiger. Claims 32-35, 52, and 64 depend from, and incorporate all the limitations of, Claim 1. Thus, Claims 32-25, 52, and 64 are patentable for at least the reasons provided above and for the additional limitations recited therein.

**CONCLUSION**

This response is being submitted on or before March 27, 2008, making this a timely response. It is believed that no additional fees are due in connection with this filing. However, the Commissioner is authorized to charge any additional fees, including extension fees or other relief which may be required, or credit any overpayment and notify us of same, to Deposit Account No. 04-1420.

This application now stands in allowable form and reconsideration and allowance are respectfully requested.

Respectfully submitted,

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